

Application/Control Number: 09/002,710
Art Unit: 1617

Page 2

CLMPTO

042503

HKD

100504

CLAIMS 1-49 (CANCELED)

CLAIMS 50-97 (ORIGINAL)

- 50. A contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids. --
- 51. A contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable gas that is a halogenated hydrocarbon, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids. --
- 52. A contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is a freon, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids. --
- 53. A contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising SF₆, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids. --
- 54. A contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is C₄F₈, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids. --

- 55. A contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is C_4F_{10} , said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids. --
- 56. A contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is CF_4 , said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids. --
- 57. A contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is SF_6 , C_4F_8 , C_4F_{10} , or CF_4 , said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids. --
- 58. A contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising a physiologically acceptable fluorinated gas and said microballoons comprising a polymer membrane wall. --
- 59. A contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising a physiologically acceptable gas that is a halogenated hydrocarbon, and said microballoons comprising a polymer membrane wall. --
- 60. A contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising a physiologically acceptable fluorinated gas that is a freon, and said microballoons comprising a polymer membrane wall. --
-
- 61. A contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising SF_6 , and said microballoons comprising a polymer membrane wall. --
- 62. A contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising C_4F_8 , and said microballoons comprising a polymer membrane wall. --
- 63. A contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising C_4F_{10} , and said microballoons comprising a polymer membrane wall. --

- 64. A contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising CF_4 , and said microballoons comprising a polymer membrane wall. --
- 65. A contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising SF_6 , C_4F_8 , C_4F_{10} , or CF_4 , and said microballoons comprising a polymer membrane wall. --
- 66. A method of ultrasonic imaging comprising:
 - administering to a subject a contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids; and
 - ultrasonically imaging said subject. --
- 67. A method of ultrasonic imaging comprising:
 - administering to a subject a contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable gas that is a halogenated hydrocarbon, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids; and
 - ultrasonically imaging said subject. --
- 68. A method of ultrasonic imaging comprising:
 - administering to a subject a contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is a freon, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids; and
 - ultrasonically imaging said subject. --

-- 69. A method of ultrasonic imaging comprising:

administering to a subject a contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising SF₆, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids; and --

ultrasonically imaging said subject. --

-- 70. A method of ultrasonic imaging comprising:

administering to a subject a contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is C₄F₈, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids; and

ultrasonically imaging said subject. --

-- 71. A method of ultrasonic imaging comprising:

administering to a subject a contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is C₄F₁₀, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids; and

ultrasonically imaging said subject. --

-- 72. A method of ultrasonic imaging comprising:

administering to a subject a contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is CF₄, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids; and

ultrasonically imaging said subject. --

-- 73. A method of ultrasonic imaging comprising:

administering to a subject a contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is SF₆, C₄F₈, C₄F₁₀, or CF₄, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids; and

ultrasonically imaging said subject. --

-- 74. A method of ultrasonic imaging comprising:

administering to a subject a contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising a physiologically acceptable fluorinated gas and said microballoons comprising a polymer membrane wall; and

ultrasonically imaging said subject. --

-- 75. A method of ultrasonic imaging comprising:

administering a contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising a physiologically acceptable gas that is a halogenated hydrocarbon, and said microballoons comprising a polymer membrane wall; and

ultrasonically imaging said subject. --

-- 76. A method of ultrasonic imaging comprising:

administering to a subject a contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising a physiologically acceptable fluorinated gas that is a freon, and said microballoons comprising a polymer membrane wall; and

ultrasonically imaging said subject. --

-- 77. A method of ultrasonic imaging comprising:

administering to a subject a contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising SF₆, and said microballoons comprising a polymer membrane wall; and

ultrasonically imaging said subject. --

-- 78. "A method of ultrasonic imaging comprising:

administering to a subject a contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising C_4F_8 , and said microballoons comprising a polymer membrane wall; and

ultrasonically imaging said subject. --

-- 79. A method of ultrasonic imaging comprising:

administering to a subject a contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising C_4F_{10} , and said microballoons comprising a polymer membrane wall; and

ultrasonically imaging said subject. --

-- 80. A method of ultrasonic imaging comprising:

administering to a subject a contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising CF_4 , and said microballoons comprising a polymer membrane wall; and

ultrasonically imaging said subject. --

-- 81. A method of ultrasonic imaging comprising:

administering to a subject a contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising SF_6 , C_4F_8 , C_4F_{10} , or CF_4 , and said microballoons comprising a polymer membrane wall; and

ultrasonically imaging said subject. --

-- 82. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids, the method comprising:

forming the stabilized microbubbles in the presence of said gas. --

Art Unit: 1617

-- 83. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable gas that is a halogenated hydrocarbon, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids, the method comprising:

forming the stabilized microbubbles in the presence of said gas. --

-- 84. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is a freon, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids, the method comprising:

forming the stabilized microbubbles in the presence of said gas. --

-- 85. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising SF₆, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids, the method comprising:

forming the stabilized microbubbles in the presence of said gas. --

-- 86. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is C₄F₈, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids, the method comprising:

forming the stabilized microbubbles in the presence of said gas. --

-- 87. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is C₄F₁₀, said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids, the method comprising:

forming the stabilized microbubbles in the presence of said gas. --

- 88. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is CF_4 , said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids, the method comprising:
 - forming the stabilized microbubbles in the presence of said gas. --
- 89. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of stabilized microbubbles, said stabilized microbubbles comprising a physiologically acceptable fluorinated gas that is SF_6 , C_4F_8 , C_4F_{10} , or CF_4 , said stabilized microbubbles being stabilized at least in part by a film-forming surfactant, and said film-forming surfactant comprising one or more phospholipids, the method comprising:
 - forming the stabilized microbubbles in the presence of said gas. --
- 90. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising a physiologically acceptable fluorinated gas and said microballoons comprising a polymer membrane wall, the method comprising:
 - forming the microballoons in the presence of at least one physiologically acceptable fluorinated gas or filling the microballoons with at least one physiologically acceptable fluorinated gas. --
- 91. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising a physiologically acceptable gas that is a halogenated hydrocarbon, and said microballoons comprising a polymer membrane wall, the method comprising:
 - forming the microballoons in the presence of at least one physiologically acceptable fluorinated gas or filling the microballoons with at least one physiologically acceptable fluorinated gas. --
- 92. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising a physiologically acceptable fluorinated gas that is a freon, and said microballoons comprising a polymer membrane wall, the method comprising:

forming the microballoons in the presence of at least one physiologically acceptable fluorinated gas or filling the microballoons with at least one physiologically acceptable fluorinated gas. --

- 93. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising SF₆, and said microballoons comprising a polymer membrane wall, the method comprising:

forming the microballoons in the presence of at least one physiologically acceptable fluorinated gas or filling the microballoons with at least one physiologically acceptable fluorinated gas. --

- 94. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising C₄F₈, and said microballoons comprising a polymer membrane wall, the method comprising:

forming the microballoons in the presence of at least one physiologically acceptable fluorinated gas or filling the microballoons with at least one physiologically acceptable fluorinated gas. --

- 95. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising C₄F₁₀, and said microballoons comprising a polymer membrane wall, the method comprising:

forming the microballoons in the presence of at least one physiologically acceptable fluorinated gas or filling the microballoons with at least one physiologically acceptable fluorinated gas. --

- 96. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas comprising CF₄, and said microballoons comprising a polymer membrane wall, the method comprising:

forming the microballoons in the presence of at least one physiologically acceptable fluorinated gas or filling the microballoons with at least one physiologically acceptable fluorinated gas. --

- 97. A method of making a contrast agent for ultrasonic echography, said contrast agent comprising an aqueous suspension of gas-filled microballoons, said gas

comprising SF_6 , C_4F_8 , C_4F_{10} , or CF_4 , and said microballoons comprising a polymer membrane wall, the method comprising:

forming the microballoons in the presence of at least one physiologically acceptable fluorinated gas or filling the microballoons with at least one physiologically acceptable fluorinated gas. --

ADD NEW CLAIMS 98-115

98. (New) A method of ultrasound imaging of the left ventricle of the heart of a subject consisting of:

- (a) suspending hydrogenated soya lecithin, dicetylphosphate and lactose in solution in the presence of C_4F_8 gas to form a gas-filled microbubble suspension;
- (b) administering portions of the gas-filled microbubble suspension to the subject;

Art Unit: 1617

- (c) applying ultrasound to the subject;
- (d) obtaining an ultrasound image of the left ventricle of the heart of the subject.

99. (New) The method of claim 98 wherein said lecithin is in lamellar or laminar form and stabilizes the microbubble boundary at the gas to liquid interface.

100. (New) A method of ultrasound imaging of the left ventricle of the heart of a subject consisting of:

- (a) suspending hydrogenated soya lecithin, dicetylphosphate and lactose in solution in the presence of CF_4 gas to form a gas-filled microbubble suspension;
- (b) administering portions of the gas-filled microbubble suspension to the subject;
- (c) applying ultrasound to the subject;
- (d) obtaining an ultrasound image of the left ventricle of the heart of the subject.

101. (New) The method of claim 100 wherein said lecithin is in lamellar or laminar form and stabilizes the microbubble boundary at the gas to liquid interface.

102. (New) A method of ultrasound imaging of the left ventricle of the heart of a subject consisting of:

- (a) suspending hydrogenated soya lecithin, dicetylphosphate and lactose in solution in the presence of C_4F_{10} gas to form a gas-filled microbubble suspension;
- (b) administering portions of the gas-filled microbubble suspension to the subject;
- (c) applying ultrasound to the subject;

(d) obtaining an ultrasound image of the left ventricle of the heart of the subject.

103. (New) The method of claim 102 wherein said lecithin is in lamellar or laminar form and stabilizes the microbubble boundary at the gas to liquid interface.

104. (New) A method of ultrasound imaging of the left ventricle of the heart of a subject consisting of:

(a) suspending hydrogenated soya lecithin, dicetylphosphate and lactose in solution in the presence of a physiologically compatible gas to form a gas-filled microbubble suspension, said gas selected from the group consisting of CF_4 , C_4F_8 and C_4F_{10} ;

(b) administering portions of the gas-filled microbubble suspension to the subject;

(c) applying ultrasound to the subject;

(d) obtaining an ultrasound image of the left ventricle of the heart of the subject.

105. (New) The method of claim 104 wherein said lecithin is in lamellar or laminar form and stabilizes the microbubble boundary at the gas to liquid interface.

106. (New) A method of ultrasound imaging of the left ventricle of the heart of a subject consisting of:

(a) suspending dipalmitoylphosphatidyl glycerol, a copolymer of polyoxyethylene-polyoxypropylene with a molecular weight of 8400 and glycerol in solution in the presence of C_4F_8 gas to form a gas-filled microbubble suspension;

(b) administering portions of the gas-filled microbubble suspension to the subject;

- (c) applying ultrasound to the subject;
- (d) obtaining an ultrasound image of the left ventricle of the heart of the subject.

107. (New) The method of claim 106 wherein said dipalmitoylphosphatidyl glycerol is in lamellar or laminar form and stabilizes the microbubble boundary at the gas to liquid interface.

108. (New) A method of ultrasound imaging of the left ventricle of the heart of a subject consisting of:

- (a) suspending dipalmitoylphosphatidyl glycerol, a copolymer of polyoxyethylene-polyoxypropylene with a molecular weight of 8400 and glycerol in solution in the presence of CF_4 gas to form a gas-filled microbubble suspension;
- (b) administering portions of the gas-filled microbubble suspension to the subject;
- (c) applying ultrasound to the subject;
- (d) obtaining an ultrasound image of the left ventricle of the heart of the subject.

109. (New) The method of claim 108 wherein said dipalmitoylphosphatidyl glycerol is in lamellar or laminar form and stabilizes the microbubble boundary at the gas to liquid interface.

110. (New) A method of ultrasound imaging of the left ventricle of the heart of a subject consisting of:

- (a) suspending dipalmitoylphosphatidyl glycerol, a copolymer of polyoxyethylene-polyoxypropylene with a molecular weight of 8400 and glycerol in solution in the presence of C_4F_{10} gas to form a gas-filled microbubble suspension;

Art Unit: 1617

- (b) administering portions of the gas-filled microbubble suspension to the subject;
- (c) applying ultrasound to the subject;
- (d) obtaining an ultrasound image of the left ventricle of the heart of the subject.

111. (New) The method of claim 110 wherein said dipalmitoylphosphatidyl glycerol is in lamellar or laminar form and stabilizes the microbubble boundary at the gas to liquid interface.

112. (New) A method of ultrasound imaging of the left ventricle of the heart of a subject consisting of:

- (a) suspending dipalmitoylphosphatidyl glycerol, a copolymer of polyoxyethylene-polyoxypropylene with a molecular weight of 8400 and glycerol in solution in the presence of a physiologically compatible gas to form a gas-filled microbubble suspension, said gas selected from the group consisting of CF_4 , C_4F_8 and C_4F_{10} ;
- (b) administering portions of the gas-filled microbubble suspension to the subject;
- (c) applying ultrasound to the subject;
- (d) obtaining an ultrasound image of the left ventricle of the heart of the subject.

113. (New) The method of claim 112 wherein said dipalmitoylphosphatidyl glycerol is in lamellar or laminar form and stabilizes the microbubble boundary at the gas to liquid interface.

114. (New) A method of ultrasound imaging of the left ventricle of the heart of a subject consisting of:

(a) sonicating human serum albumin in solution in the presence of CF_4 gas to form a microballoon suspension which microballoons are bounded by a material envelope formed with the albumin and are filled with the gas;

- (b) administering portions of the microballoon suspension to the subject;
- (c) applying ultrasound to the subject;
- (d) obtaining an ultrasound image of the left ventricle of the heart of the subject.

115. (New) A method of ultrasound imaging of the left ventricle of the heart of a subject consisting of:

(a) sonicating human serum albumin in solution in the presence of a physiologically compatible gas to form a gas-filled microballoon suspension, said gas selected from the group consisting of CF_4 , C_4F_8 and C_4F_{10} and which microballoons are bounded by a material envelope formed with the albumin and are filled with the gas;

- (b) administering portions of the microballoon suspension to the subject;
- (c) applying ultrasound to the subject;
- (d) obtaining an ultrasound image of the left ventricle of the heart of the subject.